# CALIFORNIA DEPARTMENT PESTICIDE REGULATION MEDICAL TOXICOLOGY BRANCH

# SUMMARY OF TOXICOLOGY DATA

LINURON

SB 950-140, Tolerance # 184 Chemical Code #: 000361

> September 18, 1987 Revised: 3/20/90, 3/22/91, 9/30/93

# I. DATA GAP STATUS

Combined (Chronic + Onco) rat: No data gap, possible adverse effect

Chronic rat: (See combined rat, above)

Chronic dog: No data gap, possible adverse effect

Onco rat: (See combined rat, above)

Onco mouse: No data gap, possible adverse effect

Repro rat: No data gap, possible adverse effect

Terato rat: No data gap, no adverse effect

Terato rabbit: No data gap, no adverse effect

DPR MEDICAL TOXICOLOGY Page 2 LINURON

T930930

Gene mutation: No data gap, no adverse effect

No data gap, no adverse effect

DNA damage: No data gap, no adverse effect

Neurotox: Not required at this time.

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# Note, Toxicology one-liners are attached

All record numbers through 067 092520 examined.

\*\* indicates an acceptable study.

Bold face indicates a possible adverse effect.

File name: T930930

Chromosome:

Toxicology summary updated by H. Green and M. Silva, 3/20/90; Kishiyama & Silva, 3/22/91; Silva, 9/30/93.

Reconciled with library listing through record # 092520, volume 067.

THIS DOCUMENT CONTAINS SUMMARIES ONLY. FOR DETAIL, PLEASE SEE INDIVIDUAL WORKSHEETS.

#### II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

#### COMBINED, RAT

\*\*184-030/031, 036249, 036250 "Long-term Feeding Study in Rats With 3-(3,4-Dichlorophenyl)-1-methoxy--1-methyl urea," Haskell Lab. Report No. 100-80, 2/14/80. Linuron technical (97% a.i., identification N.B. 7673-8). 0, 50, 125 or 625 ppm in the diet of rats over 24 months, 80 Charles river CD rats/sex/group, interim sacrifice of 10 rats/sex/group at 12 months. Possible adverse effect: testicular interstitial cell adenomas increased in 125 and 625 ppm males, dose related. Various indications of blood cell destruction and turnover, both sexes, at 125 and 625 ppm. NOEL for chronic systemic effects = 50 ppm. Complete, ACCEPTABLE. (C. Aldous, 12/2/85).

EPA one-liner (030/031:036249, 036250): Significant increases (p < 0.05) in interstitial cell adenoma in testes of male rats receiving 125 and 625 ppm. NOEL < 50 ppm (increased MLV, decreased RBC count, possible reticulo- cytosis). Core grade = Minimum.

184-008, 027208 Summary of 030/031:036249, 036250.

184-003, 931131 Very brief summary of 030/031:036249, 036250.

#### CHRONIC, RAT

(See also Combined, Rat; above)

184-028, 036240 "Chronic Feeding Studies of Linuron (Herbicide 326) in Rats," University of Rochester School of Medicine & Dentistry, 11/12/62. Linuron technical (Herbicide 326, purity

not indicated). 0, 25, 125 or 625 ppm in 35 rats/group/sex. **Possible adverse effect indicated:** Findings of testicular tumors, hemosiderin pigments in spleen, increased erythroid endometrial hyperplasia--all at 625 ppm. Incomplete, UNACCEPTABLE--Not upgradeable (high incidence intercurrent disease resulting in too few animals/group at study conclusion). (DPR review C. Aldous 11/25/85).

EPA one-liner (028:036240): NOEL = 125 ppm (Spleen and bone marrow changes indicative of hemolysis; increased mortality, growth retardation). Core grade not stated.

184-009, 043461, 027217 "Oral Toxicity of Linuron in Rats and Dogs" (<u>Fd. Cosmet. Toxicol.</u> 6, pp. 171-183, 1968). Literature review article which contains some summary data of 028:036240.

#### CHRONIC, DOG

184-029, 036246 "Chronic Feeding Studies of Linuron (Herbicide 326) in Dogs," Univ. of Rochester School of Med. & Dentistry, 2/1/63. Test article given as H-326, assumed to be technical linuron (not otherwise specified). 0, 25, 125 or 625 ppm in diet of 3 beagles/sex/group for 2 years. Possible adverse effect indicated: Toxicity was primarily blood effects. Pigment accumulation in Kupffer cells, presumed sulfhemoglobin formation. Erythroid cell proliferation in marrow suggest RBC death and increased turnover. Apparent NOEL = 25 ppm. Incomplete, UNACCEPTABLE -Not upgradeable. (DPR review 12/3/85 C. Aldous).

EPA one-liner [ref 029:036246]: NOEL < 25 ppm: 2/6 animals showed abnormal blood pigment (oxyhemoglobin). Decreased RBC in females at 125 ppm. Decreased RBC, Hct, Hb in males at 625 ppm. Core grade not stated.

184-009, 043464, 027219 "Oral Toxicity of Linuron in Rats and Dogs" (<u>Fd. Cosmet.</u> <u>Toxicol.</u> 6, pp. 171-183, 1968). Literature review article which contains some summary data of 029:036246 in 184-029.

\*\*062 071438, "Chronic Toxicity Study with IN Z326-118, One-Year Feeding Study in Dogs", (Haskell Laboratory for Toxicology and Industrial Medicine, report # 181-88, 10/28/88). INZ-326-118 (linuron; 93.3% to 96.2% pure) was fed in the diet for 376 to 380 days at 0, 10, 25, 125 or 625 ppm to 4 Beagle dogs/sex/group. Possible adverse effect. NOEL = 25 ppm (increased relative liver weights were observed in 625 ppm males; elevated concentrations of methemoglobin and sulfhemoglobin were reported in both sexes at 125 and 625 ppm indicating a increase in hemolysis was occurring; increased hematopoietic cells in bone marrow in both sexes were observed at 625 ppm). ACCEPTABLE. (Green & Silva, 3/16/90).

# ONCOGENICITY, RAT

184-046 059704 (Ancillary rat oncogenicity study related to 184-030/031:036249, 036250). Report entitled: "Effects of Linuron Fed to Aged Male Rats" (HLR #394-86). Haskell Labs,

9/24/86. Male Crl:CD (SD)BR rats were divided into 3 groups of 25 each. One group was fed control feed and sacrificed at 2 years. One group was fed control feed for 18 months, followed by 625 ppm linuron for 6 months, and then sacrificed. The last group was fed control feed for 1 year, then 625 ppm linuron for 1 year, and was sacrificed. Both linuron treated groups lost significant weight at onset of treatment, and weighed 21 to 23% less than controls at term. There were no major effects on clinical observations, nor on mortality. Possible adverse effect indicated: Controls, 6-month treated, and 12-month treated groups had testicular interstitial cell (ISC) tumor incidence of 0, 2, and 6, respectively, and ISC hyperplasia incidence of 6, 7, and 14, respectively. Data are consistent with results of the primary rat combined study. (NLH/C. Aldous, 9/4/87).

## ONCOGENICITY, MOUSE

\*\*184-032/033, 036251, 036252 "Long-term Feeding Study With 3-(3,4-Dichlorophenyl)-1-methoxy-1-methyl urea (Lorox; Linuron; INZ-326) in Mice," Haskell Report No. 758-82, Haskell Lab., 12/22/82. Linuron, technical (97%). 0, 50, 150 1500 ppm in the diet of 80 CD-1 mice/group over 24 months. NOEL = 150 ppm. Possible adverse effect: Females at 1500 ppm had an increase in hepatocellular adenomas. Other hepatic lesions (incl. hepatocytomegaly, vacuolation, cytoplasmic alteration to pale cytoplasm) were seen in both sexes at 1500 ppm. ACCEPTABLE (missing information noted in first DPR review were addressed in registrant rebuttal of 12/9/86). (DPR reviews 12/4/85 & 9/3/87 by C. Aldous).

184-045, 051352 Supplemental data to 032/033:036251, 036252 (individual histopathology and organ weights data as part of registrant rebuttal of 12/9/86). Additional comments in Vol. 044, Tab 7.

184-008, 027209 Partial duplicate of 032/033:036251, 036252 (25 pp). Brief review by J. Christopher on 5/7/85.

# REPRODUCTION, RAT

\*\* 052, 038 090707, 086709, "Reproductive and Fertility Effects with IN Z326-118 (Linuron) Multigeneration Reproduction Study in Rats", (L. S. Mullin, E. I. Du Pont de Nemours and Co., Haskell Laboratory, HLR Report No. 20-90, 3/29/90). IN Z326-118 (Linuron, purity 96.2%, batch #: IN Z326-118) was administered in the feed at concentrations of 0 (diet), 12.5, 100, or 615 ppm and fed to 30 Crl:CD\*Br, Pl and Fl rats/sex/group (at weaning) and daily until offspring weaning. Parental NOEL = 12.5 ppm/day (Decreased body weight and food consumption at > 100 ppm was observed for both sexes of Pl & Fl). Adverse effects: Reproductive NOEL = 100 ppm (Abnormalities of the testes were observed as: small in size with atrophy, granuloma fibrosis, and hyperplasia. Epididymides were small and deformed, showing arteritis, inflammation/tubular degeneration, lymphoid foci, and oligospermia. In addition, increased estradiol and luteinizing hormone (LH) levels at 625 ppm suggest a potential for

antiandrogenic activity of linuron which correlates with **decreased fertility** for F1 parents at 625 ppm (not statistically significant--72.4% in control compared with 53.6% at 625 ppm). Ocular lesions (corneal opacity in 3/30 males and 1/29 females, lens degradation in 3/30 males and 2/29 females, and corneal focal mineralization) occurred in F1 at 625 ppm.) Pup NOEL = 100 ppm/day (Decreased pup weights, **litter size (F2)**, and pup viability was observed at 625 ppm). ACCEPTABLE (The report is acceptable despite the fact that pages 499-500 are missing.) (Kishiyama, & Silva, 3/7/91).

065 092520, Additional information to DPR document 052 090707 (HLR 20-90). "Investigation of a Mechanism for Leydig Cell Tumorigenesis by Linuron in Rats", (J. C. Cook, E.I. du Pont de Nemours and Co., Haskell Laboratory for Toxicology and Industrial Medicine, HL report No. 494-90, 9/10/90). IN Z326 (linuron), purity = 96.2%, was administered by oral gavage at a concentration of 200 mg/kg/day to 10 "growing" (33-46 days of age) and 10 adult (93-107 days of age) male rats for 14 days. Four groups, each with 10 males, served as

test article vehicle (methocel\*), positive control vehicle (arachis oil/benzyl alcohol mix), pair-fed, and positive (flutamide) controls, respectively. Data suggest linuron inhibits testosterone. Epididymides, accessory sex organ unit (androgen-dependent tissue), prostate, ventral prostate and seminal vesicles had decreased weights when compared to vehicle controls. The level of luteinizing hormone (LH) increased and was possibly the triggering mechanism for Leydig cell hyperplasia and/or adenoma formation. In vitro test results indicate linuron is able to compete for and bind to an androgen receptor. (Kishiyama & Silva, 3/10/91).

184-067 089571 Addendum to "Reproductive and Fertility Effects with IN Z326-118 Multi-Generation Reproduction Study in Rats," (Stula, E.F., E.I. du Pont de Nemours and Company, Haskell Laboratory for Toxicology & Industrial Medicine, Newark, DE, 3/29/90). According to the report, the study was performed to more thoroughly examine the eye lesions reported in DPR volume/record #'s: 038 & 052/086709 & 090707. Originally it was reported that eye lesions in F1 male & female rats at 625 ppm might be compound related. After reevaluation, it appears that ocular effects are compound related in both sexes, but to a lesser degree in females than males (degeneration/basophilia of the cornea & other effects) at 625 ppm. These data are supplemental. Possible adverse effects. NOEL for eye effects = 100 ppm. M. Silva, 9/23/93.

184-034, 036253 "Multigeneration Reproduction Study in Rats With 3-(3,4-Dichlorophenyl)-1-methoxy-1-methylurea (Lorox, Linuron, INZ-326)," Project No. 4581-001, Haskell Lab., 10/26/84. Linuron technical (94.5% purity). 0, 25, 125, 625 ppm in the diet of 20 rats/sex/group. A three generation study with 5 litters. Possible adverse effect indicated: Apparent parental effects NOEL = 25 ppm (weight gain decrements in females at 125 and 625 ppm and in males at 625 ppm). Apparent NOEL for reproduction/lactation parameters = 125 ppm (smaller litters, reduced 24 hour survival of pups, reduced pup weights). Incomplete, UNACCEPTABLE--Not Upgradeable (No microscopic evaluation of adult animals, even of those which indicated reproductive toxicity. Insufficient clinical observations). (DPR review 12/6/85 C. Aldous).

EPA one-liner (034:036253): Reproductive NOEL = 25 ppm. Reproductive LEL = 125 ppm (lower weanling weights). Pup weights more consistently reduced at 625 ppm (days 1-21). Liver and kidney weights reduced at 625 ppm. Liver atrophy at 625 ppm. Also, lower

fertility, reduced pup survival on days 0-4 in 625 ppm groups. Systemic NOEL (adults) = 25 ppm. Systemic LEL (adults) = 125 ppm (reduced weights and weight gains of dams prior to mating, reduced dam weights at weaning). Reduced body weight gains of both sexes and alopecia at 625 ppm. Core grade = Supplementary.

184-034, 036254 "Cross-mating Study With INZ-326," Haskell Lab., 8/8/85. Linuron technical (94.5% purity). High dose (625 ppm) and control rats of a previous study (034:36253) cross-mated twice different partners to yield F3B and F3C offspring. Possible adverse effect indicated: Fertility was low in all combinations. Incidence of sperm plugs and percent pregnancy was lower in F3B litters when the treated males were cross-mated with controls than when control males were cross-mated with high-dose females. There was no such difference in F3C litters. Ancillary study does not answer questions raised in 034:36253, and a new reproduction study is required. UNACCEPTABLE--Not upgradeable. (DPR review 12/6/85 C. Aldous).

184-028, 036241 "Reproduction Studies, Herbicide 326," Univ. of Rochester School of Medicine and Dentistry, 11/12/62. Linuron technical (Herbicide 326, purity not given). Doses tested were 0, 125 ppm in (presumably) Rochester strain rats (Wistar derived). No toxicity observed. Incomplete, UNACCEPTABLE--Not Upgradeable (MTD not achieved, only one dose level). (DPR review 11/25/85 C. Aldous).

EPA one-liner (028:036241): Reproductive NOEL > 125 ppm (Decreased litter weights in F2 & F3. Core grade not stated.

184-009, 027216 "Oral Toxicity of Linuron in Rats and Dogs" (Fd. Cosmet. Toxicol. Vol. 6, pp. 171-183). Literature review article which contains summary data of 028:036241.

184-046, 051353 (Ancillary study related to 184-034:036253). "Biochemical and Pathological Effects of Linuron in Selected Tissues of Male and Female Rats, HLR 643-86", Haskell Lab., 10/6/86. Small numbers of F and F males and female offspring of the principal reproduction study (034:036253) were maintained on respective diets (Control, 25, 125, and 625 ppm) until scheduled sacrifice at 2 years. Organs and tissues closely associated with reproductive function were examined grossly and microscopically in some of these rats . Some in vitro studies were performed to evaluate effects of linuron and its metabolites on activities of 5 testicular interstitial cell (ISC) enzymes. Blood clearance of testosterone, and ISC cell responsiveness to luteinizing hormone (LH) stimulation were the other major parameters examined. Results (Possible adverse effect indicated): Major microscopic findings in these aged animals included interstitial cell adenomas and ISC hyperplasia, which were both increased substantially in 125 and 625 ppm males. Uterine findings in females included cystic endometrial hyperplasia", which appeared to be dose-related and without an apparent" NOEL, and incidence of "cervical cystic hyperkeratosis", which was apparently elevated at 625 ppm. In biochemical studies, some ISC enzymes were inhibited by linuron, particularly desmolase. ISC response to LH was decreased by a 7-day regimen of 200 mg/kg/day linuron, however LH response of ISCs **increased** on chronic exposure of males to linuron, suggesting a compensatory response. These data do not allow establishment of a NOEL for reproductive effects, and an additional study is needed. (C. Aldous, 9/8/87).

## TERATOGENICITY, RAT

\*\*184-020/035, 014805, 036411 "Teratogenicity Study of 3-(3,4-Dichlorophenyl)-1-methoxy-1-methylurea in Rats," Report No. 33-79, Haskell Lab., 5/8/79. Linuron (97%), 0, 50, 125 or 625 ppm in the diet days 6-15 of gestation to 27 mated rats/group. Maternal effects NOEL = 125 ppm (reduced body weight gain: also possible maternal treatment effects limited to the 625 ppm group included one dam with chromodacryorrhea and one with a total litter loss). Developmental toxicity NOEL = 125 ppm (slight increases in minor skeletal anomalies: thoracic bipartite centra and asymmetrical sternebrae). No apparent adverse health effects indicated, as maternal toxicity and minor developmental effects were observed at the same dosage. Study not accepted by J. Christopher for 6 concerns listed in his 5/8/85 review. Study found ACCEPTABLE by C. Aldous on 9/3/87 upon examination of additional data submitted in the 12/9/86 du Pont rebuttal response. [Note: EPA accepted this as a "Guideline" study. EPA review in Vol. 044, Tab 2.]

184-044, 051351 Rebuttal comments and some additional data to 020:014805 submitted 12/9/86 (see above). Major concerns of the 5/8/85 DPR review were addressed.

111-068/084, 014778 "Teratogenicity Studies on Linuron, Malathion and Methoxychlor in Rats," Toxicol. Appl. Pharmacol. 45, 435-444 (1978). Technical linuron (95.1%) at 0, 12.5, 25, 50, 100 or 200 mg/kg. Two linuron formulations each containing 50% linuron (L2 & L3); L2 tested at 0, 50, 100 & 200 mg/kg; L3 tested at 1, 25, 50, 100 & 200 mg/kg. Oral gavage to 20 mated Wistar rats/group days 6-15 of gavage. Decrease in maternal weight gain at high dose reported, however data does not support this. Insufficient information for independent adverse effects assessment. Incomplete UNACCEPTABLE (lacks analysis of dosing solutions, individual data). DPR review 5/6/85 by J. Christopher.

# TERATOGENICITY, RABBIT

\*\*184-035, 036412 "Developmental Toxicity Study of INZ-326 Administered Via Gavage to New Zealand White Rabbits," Argus Research Lab., 9/16/85. Linuron (96.2%) at 0, 5, 25, 100 mg/kg

days 7-19 of gestation to groups of 25 New Zealand rabbits by oral gavage. Maternal and developmental toxicity NOEL = 25 mg/kg (High dose associated with decreased maternal weight gain, liver hypertrophy, and increased abortions. The only fetal effect was increased incidence of irregularly shaped fontanelle at high dose, hence not an adverse developmental effect. Complete, ACCEPTABLE. (DPR 12/9/85 C. Aldous).

184-009, 027218 "Oral Toxicity of Linuron in Rats and Dogs," <u>Fd. Cosmet. Toxicol. 6</u>, 1968, pp. 171-183. Literature review article which contains a summary of a teratology study in New Zealand rabbits. Linuron (a 50% WP formulation) at 0, 25 or 125 ppm in the diet, 8 mated does/group. Insufficient information for adverse effects assessment. Incomplete (no individual data), UNACCEPTABLE--Not Upgradeable (only 2 dose levels, no evidence of maternal toxicity). DPR review 5/6/85 by J. Christopher.

EPA one-liner (#027218): Teratogenic NOEL > 125 ppm. Core grade not

stated.

#### MUTAGENICITY STUDIES

Note: Both EPA and DPR have found one or more studies acceptable for each of the three categories of mutagenicity studies. In some cases below, gene mutation studies indicate DPR "acceptable", but with the caveat that a given study would not be acceptable by current standards. Usually this was because of lack of a repeat trial. Because there were two negative microbial assays which were individually faulted primarily for lack of a repeat trial, and one mammalian cell study which was fully acceptable to EPA and DPR, failings of the bacterial cell studies accepted previously by DPR constitute a moot issue: the data requirement is filled.

#### GENE MUTATION

184-009, 931141 "Screening of Pesticides for Mutagenic Potential Using Salmonella typhimurium", <u>J. Agric. Food Chem. (Univ. of Kentucky)</u>, 24:560-563 (1976), Linuron (no purity

stated) tested at 25 ug/plate without activation and 200 ug/plate with activation. S. typhimurium strains TA 1535, TA 1536, TA 1537, TA 1538. Rat liver S-9. Insufficient information for independent adverse effects assessment. Incomplete (no individual data\_, UNACCEPTABLE--Not upgradeable (only one dose level). DPR review 5/6/85 J. Christopher.

\*\*184-009, 027214 "Mutagenicity Testing on Linuron in Microbial Systems," Institute of Env. Tox., Tokyo, Japan, no date. Linuron (99.8%). S. typhimurium at 10, 50, 100, 500 or 1000 ug/plate tested with and without rat liver S-9. Duplicate plates. No adverse effect indicated. Complete, ACCEPTABLE. (DPR review 5/6/85 J. Christopher). (Note: This study would be considered unacceptable by current standards).

184-020, 14806 "Mutagenicity Evaluation in Salmonella typhimurium," Haskell Lab. Report No. 106-83, 2/17/83. S. typhimurium strains TA 1535, TA 1537, TA 98, TA 100. Linuron (95-97%) at 0, 0.5, 0.75, 1.0, 2.5 & 5.0 ug/plate without activation and 0, 1.0, 5.0, 10.0, 50.0 & 100 ug/plate with activation, duplicate plates; rat liver S-9. Insufficient information for independent adverse effects assessment. Incomplete (missing cytotoxicity data), UNACCEPTABLE--upgradeable (need justification of dose selection). DPR review J. Christopher 5/7/85.

EPA one-liner (020:14806): Uniformly negative. Core grade = Acceptable.

184-009, 931140 Summary information.

184-035, 36407 Duplicate pages of 020:14806 plus 2 pages of statistical analyses.

184-009, 027212 "Mutagenicity Testing on Linuron in Microbial Systems," Institute of Env. Tox., Tokyo, Japan, no date. Linuron (99.8%). S. typhimurium strain G46; Host mediated assay with male ICR mice. 0, 50, 200 mg/kg by oral gavage. No adverse effect indicated. Incomplete (missing individual data), UNACCEPTABLE--Not upgradeable (not an accepted protocol). DPR review J. Christopher 5/6/85.

\*\*184-009, 027213 "Mutagenicity Evaluation on Linuron in Microbial Systems," Institute of Env. Tox., Tokyo, Japan, no date. Linuron (99.8%) at 0, 10, 50, 100, 500 & 1000 ug/plate, duplicate plates; E. coli WP2 hcr. No adverse effect indicated. Complete, ACCEPTABLE. DPR review J. Christopher 5/6/85. (Note: This study not acceptable by current standards).

\*\*184-020, 014808 "CHO/HGPRT Assay For Gene Mutation," Haskell Lab., Newark, Delaware, 10/11/83. Chinese Hamster Ovary cells, strain BH4 clone of CHO-K1. Linuron (94.5%) at 0.05, 0.25, 0.35, 0.40, 0.45 & 0.50 mM without activation and at 0.25, 0.50, 0.75, 0.90 & 1.00 with activation; rat liver S-9. No evidence of mutagenicity in the absence of cytotoxicity. Complete, ACCEPTABLE. DPR review 5/7/85 J. Christopher.

EPA one-liner (020:14808): Uniformly negative. Core grade = Acceptable.

184-009, 027210, 027211 "Evaluation of Herbicides for Possible Mutagenic Properties", <u>J. Agr. Food Chem.</u>, Vol. 20, No. 3, 1972. Linuron (50%) tested along with 109 other herbicides in two reverse mutation assay systems: S. typhimurium and T4 bacteriophage (E. coli). No adverse effects indicated in report, but insufficient information provided for independent adverse effects assessment. Incomplete, UNACCEPTABLE. DPR review 5/6/85 J. Christopher.

#### CHROMOSOME ABERRATION

\*\*184-020, 014809 "In Vivo Bone Marrow Chromosome Study in Rats, H #14,703," Hazleton Lab., Vienna, VA, 9/1/83. Linuron (94.5%) at 0, 100, 300 or 1000 mg/kg to 20 Sprague-Dawley rats/sex/group in a single oral gavage dose. No adverse effect indicated. Complete, ACCEPTABLE. DPR review 5/7/85 J. Christopher.

EPA one-liner (#14809): No increases in aberration frequency. Maximum dosage usable 300 mg/kg. Core grade = acceptable.

#### DNA DAMAGE

\*\*184-020, 014807 "Unscheduled DNA Synthesis/Rat Hepatocytes In Vitro," Haskell Lab. Report No. 190-83, Newark, Delaware, 5/13/83. Linuron (94.5%) Trial 1: 10-5 to 50 mM (8 concentrations), Trial 2: 10-2 to 50 mM (5 concentrations); duplicate cultures/level. No evidence of UDS. Complete, ACCEPTABLE. DPR review 5/7/85 J. Christopher.

EPA one-liner (#14807): Negative for unscheduled DNA synthesis. Core grade = acceptable.

184-009, 027215 "Mutagenicity Testing on Linuron in Microbial Systems," Institute of Env. Tox., Tokyo, Japan, no date. Rec-assay, <u>B. subtilis</u>, Linuron (99.8%) at 20, 100, 200, 500, 1000 or 2000 ug/disk; single plates per dose level. Insufficient information for adverse effects assessment. Incomplete, UNACCEPTABLE--Not upgradeable (no metabolic activation, only one plate per level, strain not characterized). DPR review 5/6/85 J. Christopher.

# NEUROTOXICITY

Not required at this time.

DPR MEDICAL TOXICOLOGY LINURON Page 17

Т930930

MISCELLANEOUS

184-021, 022062 "Guidance For The Registration of Pesticide Products Containing Linuron," 6/29/84.